REMARKS

This submission is in response to the Office Action dated February 27, 2003. Claims 2, 5-8, 16, and 18-24 are pending in this application. Claims 11-14 have been cancelled as depending on a cancelled claim 22. Reconsideration of the above identified application in view of the following remarks is respectfully requested.

Applicants note that all of the outstanding issues have been resolved, except for the question of obviousness. Because the references themselves lead away from the invention, because the claims differ from the cited references in an unpredictable way, and because a product employing the claimed features has achieved significant commercial success in the marketplace (and the closest prior art, while patented, is not itself effective enough to constitute a commercial product), *prima facie* obvious does not obtain, and if it does the secondary evidence of unobviousness rebuts it.

UNOBVIOUSNESS OF THE INVENTION

The Examiner has rejected claims 2, 5-8, 11-14, 16, 18-21, and 23-24 as allegedly being unpatentable under 35 U.S.C. § 103(a) over U.S. Patent No. 5,183,659 ("Timoney I") in view of EP0786518 A1 ("Hartford"), and U.S. Patent No. 5.597,807 ("Estrada") as further evidenced by Timoney et al., Recent Advances in Streptococci and Streptococcal Diseases, Reedbooks Ltd., 1985: Proceedings of the IXth Lancefield International Symposium on

Streptococci and Streptococcal Diseases held in September 1984, pp. 294-5 ("Timoney II"). Applicants respectfully disagree with the Examiner's contentions.[1]

As discussed previously, the present invention is directed to compositions and methods of treatment that employ a novel combination of a live, non-encapsulated, attenuated *S. equi* and saponin, an immunostimulant that in the context of the present composition enhances mucosal immunity against *S. equi* in this composition. The prior art cited by the examiner describes a live, non-encapsulated, attenuated *S. equi*, which is in fact the strain exemplified in the present application and a limitation of claims 5, 16, and 18 (Timoney I and Timoney II); an improved attenuated, encapsulated *S. equi* strain (Hartford), and use of Qunioa saponin as either an adjuvant or as an agent to enhance mucosal absorption of a drug (Estrada). Timoney I and II, and Hartford, report data that show the *S. equi* strain is immunogenic, and suggest that the strains disclosed in each may be useful as a vaccine.

None of these references describe a commercially successful strain, and indeed the applicant discovered that although immunogenic, the Timoney I strain is not effective *on its own* as a commercially acceptable vaccine, despite the disclosure in Timoney I of just such a use. Consequently, the Timoney I strain *alone* has not been developed commercially.

Hartford, which was published in 1997, almost a decade after Timoney I's PCT publication, describes an *improved S. equi* vaccine *that still retains its capsule* (see Hartford, page 2, lines 54-56). The improvement of Hartford is a deletion of about 1kb from the *S. equi* genome, which thus greatly limits the possibility of reversion to virulence (*Id.*). Hartford

[1] As claims 11-14, which depended from cancelled claim 22 have now been cancelled, the rejection is moot with respect to these claims.

mentions the possible use of adjuvants (Timoney I does not), such as Freunds Complete and incomplete adjuvants (Freunds complete adjuvant is unacceptable for veterinary purposes), vitamin E, non-ionic block polymers, muramuldipepides, ISCOMs, Quill A (a saponin), mineral oil, vegetable oil, and Carbopol (*Id.*, page 3, lines 39-43). For mucosal applications, Hartford teaches *E. coli* heat-labile toxin (LT) or Cholera toxin (CT) (*Id.*, page 3, line 44).

Estrada teaches that Quinoa saponins are useful for eliciting humoral (IgG) and secretory (IgA) immunity (Estrada, col. 5, lines 38-44). In *addition,* "[t]he Quinoa saponins can be used as adsorption adjuvants to enhance the uptake of a substance, such as a drug, administered therewith, through, e.g., mucosal surfaces including membranes of the mouth, intestine, rectum, nose, eye and lung, among others." (*Id.*, col. 6, lines 57-62; emphasis added).

The Examiner contends that the cumulative reference teachings provide both the suggestion and the expectation of success with respect to the Applicant's claimed invention. More specifically, the Examiner contends that the references suggest the alleged improvement of the immune response and protection achieved via the Timoney vaccine with the combination of saponin. The Examiner also contends the references show use of such composition for the protective effects in horses.

Applicant respectfully disagrees. As discussed below, the references provide neither the suggestion for their combination nor a reasonable expectation of success. The Examiner's rejection fails to establish that the combined materials are effective in horses, since the only objective suggestion for such a combination for horses is found in the application under examination. Furthermore, secondary indicia of unobviousness (unexpected superiority leading

to commercial success and satisfaction of a long felt need) establish unobviousness of the invention.

The References Provide No Motivation for Their Combination

The relevant test for obviousness requires three basic factual inquiries: the scope and content of the prior art are to be determined; the differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the art resolved. *Graham v. Deere*, 383 U.S. 1, 17 (1966). The Court of Appeals for the Federal Circuit has frequently articulated its longstanding analysis of prima facie obviousness determination. See *In re Fritch*, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992). As explained in *Fritch*, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. 23 U.S.P.Q.2d at 1783, citing, *In re Piasecki*, 223 U.S.P.Q. 785, 787-88 (Fed. Cir. 1984). To satisfy this burden, the Examiner must show some objective teaching from the prior art that would lead an individual to combine relevant teachings of the references. *Id.*, citing, *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); accord, *In re Lalu*, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1988); *In re Oetiker*, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992) (Nies, J. concurring). References "must be read as a whole and consideration must be given where the references diverge and teach away from the claimed invention" when determining the scope and content of the prior art, and determining whether the prior art suggests the claimed invention. *Akzo N.V. v. United States Int'l Trade Comm'n*, 1 USPQ2d 1241, 1246 (Fed. Cir. 1986); *In re Fine*, 5 USPQ2d at 1598-99; *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984) ("In effect, [the prior art] teaches away from the board's proposed modification"). The Examiner cannot rely on hindsight to arrive at a determination of

obviousness. *Fritch*, 23 U.S.P.Q.2d at 1784. The Applicant can attack and rebut the determination of prima facie obviousness when improperly made out, as it is in the present case. *Fritch*, 23 U.S.P.Q.2d at 1783. In particular, the mere fact that the teaching of a reference may be modified so as to achieve the claimed invention does not render the claimed invention obvious unless the prior art suggested the desirability of the modification. *Fritch*, 23 U.S.P.Q.2d at 1783-4.

The Examiner's premise for the obviousness rejection depends on a combination of references that, when considered fully, provide no motivation for their combination. Indeed, the references teach away from the combination, thus precluding a determination of *prima facie* obviousness.

At the outset, there is no motivation in Timoney I or II to include an adjuvant. As the Examiner has stated, neither Timoney reference teaches or even suggests including an adjuvant. Moreover, Timoney I describes the *S. equi* 709-27 strain as a vaccine in its own right, based on experiments in ponies and horses (Timoney I, col. 5, lines 7-47) and mice (*Id.*, col. 6, lines 29-50). Most importantly, Timoney does not suggest or teach the work done by the present inventors in arriving at a successful vaccine for strangles.

The Examiner looks to Hartford to fill in this gap, but Hartford disparages the Timoney encapsulated *S. equi* strain, leading away from the combination. Hartford leads further away in describing the types of adjuvants to use for mucosal administration.

Hartford expressly teaches away from the Timoney strain (Hartford, page 2, lines 31-49):

> Only one patent (EP 0.230.456) is known, in which a vaccine based on a specific live attenuated Streptococcus equi strain is

claimed. No commercial vaccines based on this patent have been put on the market yet, although the patented strain exists for 10 years now.

The vaccine of patent EP 0.230.456, although better than the existing bacterin and sub-unit vaccines, has several drawbacks:

a) the attenuated character is based on chemically induced, non-defined mutations in the genome of the vaccine strain. These mutations are almost certainly point-mutations, due to the used mutagens: nitrosoguanidine. Point-mutations are prone to back-mutation and thus to reversion to virulence. An attenuated strain in which attenuation is caused by a well-defined irreversible deletion of a substantial size, and thus not capable of reverting to virulence would therefore be highly preferred.

b) the vaccine is based on a non-encapsulated strain: screening was done for non-encapsulated colonies. Their loss of virulence is the basis for the vaccine. As a consequence, a vaccine based thereon would thus not protect against one apparent virulence factor i.e. the capsule.

A live vaccine still comprising the capsule, and thus providing a more complete protection, would therefore be preferred.

c) the vaccine is not fully safe in foals. Since however foals are the most susceptible to the disease, they should be vaccinated at a very young age. Therefore a vaccine that is completely safe in foals should be highly advantageous.

The European Patent cited in Hartford (see page 2, lines 31 and 34) is the counterpart of Timoney I (see Exhibit 1 attached hereto).[2] Hartford teaches away from Timoney I by specifically teaching the alleged deficiencies of this patent, including (i) that after 10 years it had not yielded a commercial product; (ii) that the nature of the attenuation, using nitrosoguanidine mutagenesis, was potentially inadequate to prevent reversion to virulence; and

[2] EP 0.230.456 B1 claims priority to U.S. application Serial No. 754,613. The Timoney '659 patent issued from an application that was a continuation of 754,613. The disclosures are substantially identical, except for the text beginning at col. 3, line 62 and extending through col. 4, line 53 of the '659 patent which is not found in EP 0.230.456.

(iii) that a non-encapsulated strain would be less effective for use in a vaccine. Given these teachings, which specifically disparages the attenuated, non-encapsulated *S. equi* strain exemplified and claimed in the present invention, one of ordinary skill in the art would not have any motivation to combine Hartford's teachings with those of Timoney. On the contrary, Hartford teaches away from Timoney. See *In re Sponnoble*, 160 USPQ 237, 244 (CCPA 1969) (references taken in combination teach away since they would produce a "seemingly inoperative device"); *In re Caldwell*, 138 USPQ 243, 245 (CCPA 1963) (reference teaches away if it leaves the impression that the product would not have the property sought by the applicant). Where the prior art leads away from the claimed invention, obviousness does not obtain. See *In re Lundsford*, 148 U.S.P.Q. 721, 726 (CCPA 1966). When a reference teaches away from the claimed invention, the requisite teaching to establish *prima facie* obviousness is absent, thus precluding a conclusion of unpatentability. See *In re Bell*, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993).

Even ignoring this express teaching away, as one must to consider the next point, Hartford then discourages the use of a saponin in combination with an attenuated *S. equi* strain for mucosal administration. Hartford describes a number of adjuvants, among them Complete Freunds Adjuvant, which is potent but highly toxic, and Quill A, a saponin. There is no particular reason to select any one of them. Furthermore, the actual exemplification of the vaccine in Hartford involves a bacterin preparation without any adjuvant, and oral or parenteral administration. Hartford does, however, propose an adjuvant for use in a muscosal composition: "[a]djuvantia, specially suitable for mucosal application are e.g. the E. coli heat-labile toxin (LT) or Cholera toxin (CT)" (Hartford, page 3, line 44). Thus, to the extent Hartford teaches

compositions and methods for nasal administration, these compoisitions and methods do not involve saponin. Thus, the only motivation to combine an attenuated *S. equi* with saponin for nasal (mucosal) administration is from the disclosure of the present application, since Hartford advocates using LT or CT for such compositions.

Estrada does not supply the absent motiviation, and, like Hartford, teaches away from the claimed invention. Contrary to the Examiner's contentions, which were led to a misunderstanding of this reference by the applicants' attorneys, Estrada does not ever describe using Quinoa saponin with an antigen for nasal administration.[3] Estrada describes two novel and distinct attributes of Quinoa saponins: they "... are able to act as both immunological and absorption adjuvants to enhance immune responses and mucosal absorption, *respectively*" (Estrada, col. 2, lines 22-24; emphasis added). Estrada describes these characteristics as unrelated. Further evidence that Estrada does not teach nasal administration of an immunogen with Quinoa saponins is ample in the specification (*Id.*, col. 8, lines 25-45; emphasis added):

> The mode of administration of the Quinoa saponin compositions will vary according to the intended use. For example, if used as immunological adjuvants (e.g., in the case of a vaccine) and systemic immunity is required, the Quinoa saponin composition will generally be administered parenterally, usually by intramuscular injection. If mucosal immunity is required, the Qunioa saponin will generally be administered *enterally, usually by oral dosing or inhalation.* Other modes of

[3] In the amendment dated March 13, 2002, applicant's attorneys mistakenly stated that "Estrada teaches that saponin surprisingly stimulated an immune response when administered mucosally." (See page 6, second full paragraph). Estrada teaches no such thing.

administration, however, such as intradermal, intraperitoneal and intravenous injection, are also acceptable....

When used as absorption adjuvants, the subject compositions will generally be delivered by oral, intranasal, topical, rectal, intraocular and inhalation methods, and the like. However, such compositions can also be administered subcutaneously, intramuscularly, intradermally, and intraperitoneally.

Estrada expressly describes various modes of administration for antigens and drugs, explicitly describing intranasal administration for a drug and not a vaccine. Estrada clearly differentiates intranasal from inhalation in this passage. Most importantly, Estrada differentiates immunization from mucosal adsorption. Contrast the statement that "... the Quinoa saponins can be used as immunological adjuvants in vaccine compositions for a variety of purposes" (*Id.*, col. 6, 13-15) with "[t]he Quinoa saponins can also be used as absorption adjuvants, to enhance the uptake of a substance, such as a drug, administered therewith, through e.g., mucosal surfaces including membranes of the mouth, intestine, rectum, nose, eye and lung..." (*Id.*, col. 6, lines 57-61) in light of the passage quoted above. Estrada defines antigens, which are vaccine components, in distinction to drugs (see *Id.*, col. 4, lines 5-12). Thus, according to Estrada, Quinoa saponins are useful either as adjuvants or for enhancing mucosal administration.

The only suggestion that Quinoa saponins are useful for compositions and methods for *intranasal* administration of a *vaccine* is found in the present application, not in the prior art, and certainly not in Estrada. The rejection requires hindsight reconstruction based on the disclosure of the application under examination, which as pointed out above is improper. The

Court of Appeals for the Federal Circuit has stated that "selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings. There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the Applicant's disclosure." *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988).

Thus, the references, taken as a whole, cannot be combined as the Examiner proposes. The references defy such a combination; it violates their express disclosures. The references cannot be modified as the examiner suggests because doing so offends their express teachings. The references in no way suggest the desirability of the proposed modification. Thus, *prima facie* obvious does not obtain here.

Even If Combined, There is No Reasonable Expectation of Success

The relevant inquiry for obviousness is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicant's disclosure. *In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991). The absence of any suggestion to combine the references is clearly established above. As discussed extensively in applicant's prior amendments, there is no reasonable expectation from the references, whether taken alone or in combination, that the claimed compositions containing an attenuated, non-encapsulated *S. equi* strain and saponin, or methods using such compositions, would be effective for treating strangles.

Applicant previously submitted a Declaration Under 37 C.F.R. §1.132 of Wumin Li, Ph.D. (the "Li Declaration"), which established the unpredictability of the claimed compositions and methods (see the Amendment filed March 13, 2002). In particular, the Li Declaration states that "[a]t the time of the invention, the efficacy of saponin as an adjuvant was not predictable." (Li Declaration, ¶ 4(A)). Dr. Li describes the variable results with different adjuvants for a foot and mouth disease (FMD) in cattle, sheep, and swine (*Id.*). Dr. Li further points out that saponin preparations are widely known to have adverse biological effects, rendering them unpredictable as vaccine components. (*Id.*). Thus, "without testing the particular combination of a target antigen and saponin, one would not have been able to predict that saponin would be an effective adjuvant or that it would have a detrimental effect on the immunogenicity of the antigen." (*Id.*, ¶ 4(B)). Dr. Li is an expert in the field (Li Declaration, ¶1), and his factual assertions on these points carry considerable weight. Affidavits constitute competent evidence that cannot be ignored. See e.g., *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 U.S.P.Q. 657, 674-75 (Fed. Cir. 1985).

The Li Declaration rebuts the Examiner's conclusions of predictability based on general properties of materials by establishing unpredictability of the specific elements claimed here. It was not until the present inventor made and tested the claimed composition that one could establish that the combination would be sufficiently effective to merit actual use in horses.

The references do not supply the missing teaching necessary to establish that the claimed invention was reasonably predictable. Hartford describes combining Quill A with an encapsulated *S. equi*, an immunologically different proposition entirely from Timoney's non-ecapsulated strain, and one that in no way renders the claimed invention predictable. Estrada

describes the general properties of Quinoa saponins, without providing any basis to reasonably expect that Quinoa saponins are either safe or effective in horses, safe or effective for intranasal vaccines, and safe or effective as components in a vaccine including an attenuated, non-encapsulated *S. equi* strain. All of this could only be ascertained through the efforts of the present inventor.

The foregoing establishes that even if combined, the references do not provide a reasonable expectation of success in achieving the claimed invention. Success in this case could only come from making the invention itself, and "[p]atentability shall not be negatived by the manner in which the invention was made." 35 U.S.C. § 103(a). For this reason as well, *prima facie* obviousness does not obtain and the Examiner's rejection should be withdrawn.

Secondary Indicia of Unobviousness

The determination of obviousness is based on a series of factual considerations including (1) the scope and content of the prior art, (2) the difference between the art and the claims at issue, (3) the level of ordinary skill in the art, and (4) objective evidence of nonobviousness. *Texas Instruments, Inc. v. U.S. Int'l Trade Commission*, 988 F.2d 1165, 1178, 26 U.S.P.Q.2d 1018 (Fed. Cir. 1993). One such indicia of nonobviousness includes the claimed invention's commercial success. *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387 (Fed. Cir. 1988). An examiner cannot disregard this evidence. *Truswal Sys. Corp. v. Hydro-Air Eng'g, Inc.*, 813 F.2d 1207 (Fed. Cir. 1987).

Furthermore, even if, for the sake of argument, the references cited by the Examiner constitute *prima facie* obviousness, advantages flowing directly from the invention are

one consideration that may be relevant to a determination of obviousness. *Mosinee Paper Corp. v. James River Corp. of Virginia*, 22 U.S.P.Q.2d 1657, 1660, *aff'd. mem.* 980 F.2d 743 (Fed. Cir. 1992) (*citing Pre-Emption Devices, Inc. v. Minnesota Mining & Mfg. Co.*, 221 U.S.P.Q. 841 (Fed. Cir. 1984). "After all, those advantages are the foundation of that 'commercial success' which may be evidence of nonobviousness." *Pre-Emption, supra*, at 844 (*citing Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)).

The Declaration Under 37 C.F.R. § 1.132 of Robert Daily ("Daily Declaration") submitted with the amendment filed November 12, 2002 establishes the commercial interest, commercial success, and long felt need of the claimed invention that result from the superiority of the claimed combination. (Daily Declaration, ¶¶ 1, 2, and 3). Declarations containing evidence of commercial interest, commercial success, and long felt need must be considered by the Examiner in determining the issue of obviousness of claims for patentability under 35 U.S.C. § 103. M.P.E.P. § 716.01(a); *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995); *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983).

Mr. Daily states that the live attenuated *Streptococcus equi* and saponin composition sold under the trademark Pinnacle™ derives its commercial success from its ability to stimulate an effective protective immune response to *Streptococcus equi* in horses by contacting the cells of the nasopharyngeal mucosa, thus preventing strangles in horses. (Daily Declaration, ¶ 4). The declaration shows a clear nexus between the claimed composition, *i.e.*, a live attenuated, non-encapsulated *Streptococcus equi* in combination with saponin, and the commercial success. *Id.* Moreover, the composition was marketed to be administered through

the nasopharyngeal mucosa. *Id.* Thus, the commercial success is commensurate in scope with the claims.

Gross sales figures provide evidence of commercial success provided there is a showing as to the time period during which the product was sold, *see Ex parte Standish*, 10 U.S. P.Q.2d 1454 (Bd. Pat. App. & Inter. 1988), or a showing of evidence as to market share. *See Cable Electric Products, Inc. v. Genmark, Inc.*, 770 F.2d 1015 (Fed. Cir. 1985).

In February 1998, Applicant's live attenuated *S. equi* and saponin product was commercially introduced into the market as an alternative to a competitor's killed *S. equi* products. (Daily Declaration, ¶ 5). The declarant indicates gross sales figures in conjunction with time periods during which the Applicant's product was sold and/or indicates market share. Declarant shows that in its first year on the market, Applicant's product had gross sales in the million dollar range. *Id.* After only one year, the claimed invention had a remarkable increase of 44% in gross sales. *Id.* In 2000, the gross sales increased 30% over 1999. *Id.* 2001 showed an increase of gross sales of 13% from 2000 and as of September 2002, sales had already increased 30% over the first nine months of 2001. *Id.* Additionally, the increase of units sold yearly was dramatic. *Id.* In 1999, there was a 45% increase from the year before, while 2000 showed a 30% increase. *Id.* In 2001, there was another 5% increase of units sold and another 2.2% in 2002. *Id.* Note, too, that the value of gross sales increased faster than the number of units sold, which indicates price increases. These sales data thus show increased sales even with rising prices, thus providing ample evidence of commercial success due to product superiority.

Furthermore, the declarant states that the Applicant's claimed invention achieved gross sales greater than the competitors killed product in just its second year as a result of the

combination of the live attenuated bacterium combined with saponin, *i.e.*, the claimed subject matter of the patent application. (Daily Declaration, ¶ 6). The decrease in sales of the competition began at the time the Applicant's invention entered the market and the claimed invention significantly replaced the killed vaccine sold by those competitors. (Daily Declaration, ¶¶ 5 and 6).

Market share provides a strong indication of commercial success. *Ex parte Anderson*, 21 U.S.P.Q.2d 1241 (Bd. Pat. App. & Int. 1991). Applicant's claimed invention, from the time of its introduction into the commercial market for sale, demonstrated rapid increases in market share. In addition, the declarant states that while the Applicant's product had significant yearly increases in gross sales, sales of competitor's products, and thereby its market share, dramatically declined. (Daily Declaration, ¶ 5). Sales of a competitor's killed *S. equi* product, produced by Applicant's direct competitor, Bayer, declined approximately 39% from 1998 to 1999. *Id.* The declarant states that this decrease in sales of the killed vaccine resulted from the entry of the Applicant's claimed invention into the market in 1998. (Daily Declaration, ¶ 5). Thus, Applicant's superior product, which is reflected in the claims, replaced competitor's products and exhibited a strong growth in the market share. This establishes commercial success. *See Ex parte Remark*, 15 U.S.P.Q.2d 1498, 1505 (Bd. Pat. App. & Int. 1990).

Additionally the declarant, the Director of the Business Equine Unit for Fort Dodge Animal Health, states that the individuals who are responsible for the health of expensive horses, and who are the users of the claimed invention, would not adopt such a product unless it had substantial efficacy and was safe to use. (Daily Declaration, ¶ 6). Moreover, the declarant states the increase in sales reflects the superiority of the product and that the product has

"reinvented the strangles vaccine market." *Id.* These determinations support the conclusion that the superior quality of the applicant's invention over the competition establishes a clear nexus between the commercial success and the technical advance of the claimed invention. In addition, the rapid and substantial growth in sales and market share, along with the statement that Applicant's product had "reinvented" the market points to a pent-up long felt need for the claimed invention. See, *WMS Gaming Inc. v. International Game Technology*, 184 F. 3d 1339 (Fed. Cir. 1999).

The Examiner criticizes the Daily Declaration because it compares commercial success with a killed product, not a Timoney product. This is an easy one to address: the only "Timoney" product commercially available is in the present invention. The Timoney I strain, on its own as disclosed in Timoney I, was not effective enough to merit commercialization.[4] The Examiner has considered issuance of a patent for a useful invention (Timoney I) tantamount to development of a commercially effective product. However, this is clearly not the case.

In effect, the Examiner requires a comparison of the commercial success of the claimed product with a hypothetical product. However, commercial success can only be measured in the marketplace, and the comparison was made to the available commercial product, Bayer's killed *S. equi* in a Carbopol adjuvant. On the basis of superiority of the invention to this product, Dr. Chu, the inventor, recognized the advantages of the invention. (See the Declaration Under 37 C.F.R. § 1.132 of Hsien-Jue Chu submitted with the amendment filed June 29, 2001).

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[4] Were the attenuated, non-encapsulated Timoney strain sufficiently immunogenic on its own, that would be a much simpler approach to have taken. Admixing the strain with saponin, or any adjuvant, raises additional regulatory issues better, and less expensively, avoided if possible.

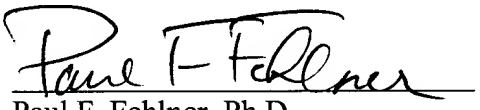
If necessary, Hartford independently establishes that Timoney I never led to a commercial vaccine in its own right (see Hartford at page 2, lines 30-33); and that such a vaccine has been needed in the art for a long time (*Id.*).

The Daily Declaration and Hartford each provides strong evidence of commercial success and satisfaction of a long felt need for an effective strangles vaccine, and clearly manifests that the invention was not obvious to those skilled in the art at the time the invention was made. When the commercial success of the claimed invention is viewed in light of the Applicant's previous arguments in conjunction with the Declarations of Dr. Chu and Dr. Li, and the discussion set forth above, it is respectfully submitted that the combination of Timoney I in view of Hartford and Estrada as further evidenced by Timoney II does not suggest making the claimed invention, nor does it provide an expectation of success, much less presage the commercial success a product of the invention has enjoyed. Therefore, the claimed invention is not obvious to one of skill in the art at the time of the invention.

CONCLUSION

For the reasons stated above, Applicant believes that the pending claims of this application are in condition for allowance. Accordingly, withdrawal of all objections and rejections and reconsideration of the application are respectfully requested. The Examiner is invited to contact Applicant's representative at the below-indicated telephone number if the Examiner believes it would advance prosecution of the application. Allowance of the claims is earnestly solicited.

Respectfully submitted,



Paul F. Fehlner, Ph.D.
Registration No. 35,135
Attorney for Applicants

DARBY & DARBY, P.C.
Post Office Box 5257
New York, NY 10150-5257
Phone (212) 527-7700